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<110> Bayer AG
Friedrich, Gabi
Hagen, Gustav
Wick, Maresa
Zubov, Dmitry
Dubois-Stringfellow, Nathalie A.

<120> METHODS FOR MODULATING ANGIOGENESIS

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<151> 1999-07-02

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Gly Ser Pro Arg Glu Phe Ile Tyr Leu Asn Arg Tyr Lys Arg Ala Gly
         35                  40                  45

Glu Ser Gln Asp Lys Cys Thr Tyr Thr Phe Ile Val Pro Gln Gln Arg
     50                  55                  60

Val Thr Gly Ala Ile Cys Val Asn Ser Lys Glu Pro Glu Val Leu Leu
 65                  70                  75                  80

Glu Asn Arg Val His Lys Gln Glu Leu Glu Leu Leu Asn Asn Glu Leu
                 85                  90                  95

Leu Lys Gln Lys Arg Gln Ile Glu Thr Leu Gln Gln Leu Val Lys Val
            100                 105                 110

Asp Gly Gly Ile Val Ser Glu Val Lys Leu Leu Arg Lys Glu Ser Arg
        115                 120                 125

Asn Met Asn Ser Arg Val Thr Gln Leu Tyr Met Gln Leu Leu His Glu
    130                 135                 140

Ile Ile Arg Lys Arg Asp Asn Ala Leu Glu Leu Ser Gln Leu Glu Asn
145                 150                 155                 160

Arg Ile Leu Asn Gln Thr Ala Asp Met Leu Gln Leu Ala Ser Lys Tyr
                165                 170                 175

Lys Asp Leu Glu His Lys Tyr Gln His Leu Ala Thr Leu Ala His Asn
            180                 185                 190

Gln Ser Glu Ile Ile Ala Gln Leu Glu Glu His Cys Gln Arg Val Pro
        195                 200                 205

Ser Ala Arg Pro Val Pro Gln Pro Pro Pro Ala Ala Pro Pro Arg Val
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Tyr Gln Pro Pro Thr Tyr Asn Arg Ile Ile Asn Gln Ile Ser Thr Asn
225                 230                 235                 240

Glu Ile Gln Ser Asp Gln Asn Leu Lys Val Leu Pro Pro Pro Leu Pro
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Thr Met Pro Thr Leu Thr Ser Leu Pro Ser Ser Thr Asp Lys Pro Ser
            260                 265                 270

Gly Pro Trp Arg Asp Cys Leu Gln Ala Leu Glu Asp Gly His Asp Thr
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Ser Ser Ile Tyr Leu Val Lys Pro Glu Asn Thr Asn Arg Leu Met Gln
    290                 295                 300

Val Trp Cys Asp Gln Arg His Asp Pro Gly Gly Trp Thr Val Ile Gln
305                 310                 315                 320

Arg Arg Leu Asp Gly Ser Val Asn Phe Phe Arg Asn Trp Glu Thr Tyr
                325                 330                 335

Lys Gln Gly Phe Gly Asn Ile Asp Gly Glu Tyr Trp Leu Gly Leu Glu
            340                 345                 350

Asn Ile Tyr Trp Leu Thr Asn Gln Gly Asn Tyr Lys Leu Leu Val Thr
        355                 360                 365

Met Glu Asp Trp Ser Gly Arg Lys Val Phe Ala Glu Tyr Ala Ser Phe
    370                 375                 380

Arg Leu Glu Pro Glu Ser Glu Tyr Tyr Lys Leu Arg Leu Gly Arg Tyr
385                 390                 395                 400

His Gly Asn Ala Gly Asp Ser Phe Thr Trp His Asn Gly Lys Gln Phe
                405                 410                 415

Thr Thr Leu Asp Arg Asp His Asp Val Tyr Thr Gly Asn Cys Ala His
            420                 425                 430

Tyr Gln Lys Gly Gly Trp Trp Tyr Asn Ala Cys Ala His Ser Asn Leu
        435                 440                 445

Asn Gly Val Trp Tyr Arg Gly Gly His Tyr Arg Ser Arg Tyr Gln Asp
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Gly Val Tyr Trp Ala Glu Phe Arg Gly Gly Ser Tyr Ser Leu Lys Lys
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Tyr Asn Arg Ile Gln His Gly Gln Cys Ala Tyr Thr Phe Ile Leu Pro
        35                  40                  45

Glu His Asp Gly Asn Cys Arg Glu Ser Thr Thr Asp Gln Tyr Asn Thr
    50                  55                  60

Asn Ala Leu Gln Arg Asp Ala Pro His Val Glu Pro Asp Phe Ser Ser
65                  70                  75                  80
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Gln Lys Leu Gln His Leu Glu His Val Met Glu Asn Tyr Thr Gln Trp
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Leu Gln Lys Leu Glu Asn Tyr Ile Val Glu Asn Met Lys Ser Glu Met
            100                 105                 110

Ala Gln Ile Gln Gln Asn Ala Val Gln Asn His Thr Ala Thr Met Leu
        115                 120                 125

Glu Ile Gly Thr Ser Leu Leu Ser Gln Thr Ala Glu Gln Thr Arg Lys
    130                 135                 140

Leu Thr Asp Val Glu Thr Gln Val Leu Asn Gln Thr Ser Arg Leu Glu
145                 150                 155                 160

Ile Gln Leu Leu Glu Asn Ser Leu Ser Thr Tyr Lys Leu Glu Lys Gln
                165                 170                 175

Leu Leu Gln Gln Thr Asn Glu Ile Leu Lys Ile His Glu Lys Asn Ser
            180                 185                 190

Leu Leu Glu His Lys Ile Leu Glu Met Glu Gly Lys His Lys Glu Glu
        195                 200                 205

Leu Asp Thr Leu Lys Glu Glu Lys Glu Asn Leu Gln Gly Leu Val Thr
    210                 215                 220

Arg Gln Thr Tyr Ile Ile Gln Glu Leu Glu Lys Gln Leu Asn Arg Ala
225                 230                 235                 240

Thr Thr Asn Asn Ser Val Leu Gln Lys Gln Gln Leu Glu Leu Met Asp
                245                 250                 255

Thr Val His Asn Leu Val Asn Leu Cys Thr Lys Glu Gly Val Leu Leu
            260                 265                 270

Lys Gly Gly Lys Arg Glu Glu Glu Lys Pro Phe Arg Asp Cys Ala Asp
        275                 280                 285

Val Tyr Gln Ala Gly Phe Asn Lys Ser Gly Ile Tyr Thr Ile Tyr Ile
    290                 295                 300

Asn Asn Met Pro Glu Pro Lys Lys Val Phe Cys Asn Met Asp Val Asn
305                 310                 315                 320

Gly Gly Gly Trp Thr Val Ile Gln His Arg Glu Asp Gly Ser Leu Asp
                325                 330                 335

Phe Gln Arg Gly Trp Lys Glu Tyr Lys Met Gly Phe Gly Asn Pro Ser
            340                 345                 350

Gly Glu Tyr Trp Leu Gly Asn Glu Phe Ile Phe Ala Ile Thr Ser Gln
        355                 360                 365

Arg Gln Tyr Met Leu Arg Ile Glu Leu Met Asp Trp Glu Gly Asn Arg
    370                 375                 380

Ala Tyr Ser Gln Tyr Asp Arg Phe His Ile Gly Asn Glu Lys Gln Asn
385                 390                 395                 400

Tyr Arg Leu Tyr Leu Lys Gly His Thr Gly Thr Ala Gly Lys Gln Ser
                405                 410                 415
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Ser Leu Ile Leu His Gly Ala Asp Phe Ser Thr Lys Asp Ala Asp Asn
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Asp Asn Cys Met Cys Lys Cys Ala Leu Met Leu Thr Gly Gly Trp Trp
        435                 440                 445

Phe Asp Ala Cys Gly Pro Ser Asn Leu Asn Gly Met Phe Tyr Thr Ala
    450                 455                 460

Gly Gln Asn His Gly Lys Leu Asn Gly Ile Lys Trp His Tyr Phe Lys
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Gln Tyr Gln Val Gln His Gly Ser Cys Ser Tyr Thr Phe Leu Leu Pro
        35                  40                  45

Glu Met Asp Asn Cys Arg Ser Ser Ser Ser Pro Tyr Val Ser Asn Ala
    50                  55                  60

Val Gln Arg Asp Ala Pro Leu Glu Tyr Asp Asp Ser Val Gln Arg Leu
65                  70                  75                  80

Gln Val Leu Glu Asn Ile Met Glu Asn Asn Thr Gln Trp Leu Met Lys
                85                  90                  95

Leu Glu Asn Tyr Ile Gln Asp Asn Met Lys Lys Glu Met Val Glu Ile
            100                 105                 110

Gln Gln Asn Ala Val Gln Asn Gln Thr Ala Val Met Ile Glu Ile Gly
        115                 120                 125

Thr Asn Leu Leu Asn Gln Thr Ala Glu Gln Thr Arg Lys Leu Thr Asp
    130                 135                 140

Val Glu Ala Gln Val Leu Asn Gln Thr Thr Arg Leu Glu Leu Gln Leu
145                 150                 155                 160

Leu Glu His Ser Leu Ser Thr Asn Lys Leu Glu Lys Gln Ile Leu Asp
                165                 170                 175

Gln Thr Ser Glu Ile Asn Lys Leu Gln Asp Lys Asn Ser Phe Leu Glu
            180                 185                 190

Lys Lys Val Leu Ala Met Glu Asp Lys His Ile Ile Gln Leu Gln Ser
        195                 200                 205
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Ile Lys Glu Glu Lys Asp Gln Leu Gln Val Leu Val Ser Lys Gln Asn
    210                 215                 220

Ser Ile Ile Glu Glu Leu Glu Lys Lys Ile Val Thr Ala Thr Val Asn
225                 230                 235                 240

Asn Ser Val Leu Gln Lys Gln Gln His Asp Leu Met Glu Thr Val Asn
                245                 250                 255

Asn Leu Leu Thr Met Met Ser Thr Ser Asn Ser Ala Lys Asp Pro Thr
            260                 265                 270

Val Ala Lys Glu Glu Gln Ile Ser Phe Arg Asp Cys Ala Glu Val Phe
        275                 280                 285

Lys Ser Gly His Thr Thr Asn Gly Ile Tyr Thr Leu Thr Phe Pro Asn
    290                 295                 300

Ser Thr Glu Glu Ile Lys Ala Tyr Cys Asp Met Glu Ala Gly Gly Gly
305                 310                 315                 320

Gly Trp Thr Ile Ile Gln Arg Arg Glu Asp Gly Ser Val Asp Phe Gln
                325                 330                 335

Arg Thr Trp Lys Glu Tyr Lys Val Gly Phe Gly Asn Pro Ser Gly Glu
            340                 345                 350

Tyr Trp Leu Gly Asn Glu Phe Val Ser Gln Leu Thr Asn Gln Gln Arg
        355                 360                 365

Tyr Val Leu Lys Ile His Leu Lys Asp Trp Glu Gly Asn Glu Ala Tyr
    370                 375                 380

Ser Leu Tyr Glu His Phe Tyr Leu Ser Ser Glu Glu Leu Asn Tyr Arg
385                 390                 395                 400

Ile His Leu Lys Gly Leu Thr Gly Thr Ala Gly Lys Ile Ser Ser Ile
                405                 410                 415

Ser Gln Pro Gly Asn Asp Phe Ser Thr Lys Asp Gly Asp Asn Asp Lys
            420                 425                 430

Cys Ile Cys Lys Cys Ser Gln Met Leu Thr Gly Gly Trp Trp Phe Asp
        435                 440                 445

Ala Cys Gly Pro Ser Asn Leu Asn Gly Met Tyr Tyr Pro Gln Arg Gln
    450                 455                 460

Asn Thr Asn Lys Phe Asn Gly Ile Lys Trp Tyr Tyr Trp Lys Gly Ser
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Gln Ile His Gln Val Arg Arg Gly Gln Cys Ser Tyr Thr Phe Val Val
        35                  40                  45

Pro Glu Pro Asp Ile Cys Gln Leu Ala Pro Thr Ala Ala Pro Glu Ala
    50                  55                  60

Leu Gly Gly Ser Asn Ser Leu Gln Arg Asp Leu Pro Ala Ser Arg Leu
65                  70                  75                  80

His Leu Thr Asp Trp Arg Ala Gln Arg Ala Gln Arg Ala Gln Arg Val
                85                  90                  95

Ser Gln Leu Glu Lys Ile Leu Glu Asn Asn Thr Gln Trp Leu Leu Lys
            100                 105                 110

Leu Glu Gln Ser Ile Lys Val Asn Leu Arg Ser His Leu Val Gln Ala
        115                 120                 125

Gln Gln Asp Thr Ile Gln Asn Gln Thr Thr Thr Met Leu Ala Leu Gly
    130                 135                 140

Ala Asn Leu Met Asn Gln Thr Lys Ala Gln Thr His Lys Leu Thr Ala
145                 150                 155                 160

Val Glu Ala Gln Val Leu Asn Gln Thr Leu His Met Lys Thr Gln Met
                165                 170                 175

Leu Glu Asn Ser Leu Ser Thr Asn Lys Leu Glu Arg Gln Met Leu Met
            180                 185                 190

Gln Ser Arg Glu Leu Gln Arg Leu Gln Gly Arg Asn Arg Ala Leu Glu
        195                 200                 205

Thr Arg Leu Gln Ala Leu Glu Ala Gln His Gln Ala Gln Leu Asn Ser
    210                 215                 220

Leu Gln Glu Lys Arg Glu Gln Leu His Ser Leu Leu Asp His Gln Thr
225                 230                 235                 240

Gly Thr Leu Ala Asn Leu Lys His Asn Leu His Ala Leu Ser Ser Asn
                245                 250                 255

Ser Ser Ser Leu Gln Gln Gln Gln Gln Gln Leu Thr Glu Phe Val Gln
            260                 265                 270

Arg Leu Val Arg Ile Val Ala Gln Asp Gln His Pro Val Ser Leu Lys
        275                 280                 285

Thr Pro Lys Pro Val Phe Gln Asp Cys Ala Glu Ile Lys Arg Ser Gly
    290                 295                 300

Val Asn Thr Ser Gly Val Tyr Thr Ile Tyr Glu Thr Asn Met Thr Lys
305                 310                 315                 320

Pro Leu Lys Val Phe Cys Asp Met Glu Thr Asp Gly Gly Gly Trp Thr
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                325                 330                 335

Leu Ile Gln His Arg Glu Asp Gly Ser Val Asn Phe Gln Arg Thr Trp
            340                 345                 350

Glu Glu Tyr Lys Glu Gly Phe Gly Asn Val Ala Arg Glu His Trp Leu
        355                 360                 365

Gly Asn Glu Ala Val His Arg Leu Thr Ser Arg Thr Ala Tyr Leu Leu
    370                 375                 380

Arg Val Glu Leu His Asp Trp Glu Gly Arg Gln Thr Ser Ile Gln Tyr
385                 390                 395                 400

Glu Asn Phe Gln Leu Gly Ser Glu Arg Gln Arg Tyr Ser Leu Ser Val
                405                 410                 415

Asn Asp Ser Ser Ser Ser Ala Gly Arg Lys Asn Ser Leu Ala Pro Gln
            420                 425                 430

Gly Thr Lys Phe Ser Thr Lys Asp Met Asp Asn Asp Asn Cys Met Cys
        435                 440                 445

Lys Cys Ala Gln Met Leu Ser Gly Gly Trp Trp Phe Asp Ala Cys Gly
    450                 455                 460

Leu Ser Asn Leu Asn Gly Ile Tyr Tyr Ser Val His Gln His Leu His
465                 470                 475                 480

Lys Ile Asn Gly Ile Arg Trp His Tyr Phe Arg Gly Pro Ser Tyr Ser
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Leu His Gly Thr Arg Met Met Leu Arg Pro Met Gly Ala
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Cys Glu Thr Leu Val Val Gln His Gly His Cys Ser Tyr Thr Phe Leu
         35                  40                  45

Leu Pro Lys Ser Glu Pro Cys Pro Pro Gly Pro Glu Val Ser Arg Asp
     50                  55                  60

Ser Asn Thr Leu Gln Arg Glu Ser Leu Ala Asn Pro Leu His Leu Gly
 65                  70                  75                  80

Lys Leu Pro Thr Gln Gln Val Lys Gln Leu Glu Gln Ala Leu Gln Asn
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Asn Thr Gln Val Leu Lys Lys Leu Glu Arg Ala Ile Lys Thr Ile Leu
            100                 105                 110
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Arg Ser Lys Leu Glu Gln Val Gln Gln Gln Met Ala Gln Asn Gln Thr
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Ala Pro Met Leu Glu Leu Gly Thr Ser Leu Leu Asn Gln Thr Thr Ala
    130                 135                 140

Gln Ile Arg Lys Leu Thr Asp Met Glu Ala Gln Leu Leu Asn Gln Thr
145                 150                 155                 160

Ser Arg Met Asp Ala Gln Met Pro Glu Thr Phe Leu Ser Thr Asn Lys
                165                 170                 175

Leu Glu Asn Gln Leu Leu Leu Gln Arg Gln Lys Leu Gln Gln Leu Gln
            180                 185                 190

Gly Gln Asn Ser Ala Leu Glu Lys Arg Leu Gln Ala Leu Glu Thr Lys
        195                 200                 205

Gln Gln Glu Glu Leu Ala Ser Glu Leu Ser Lys Lys Ala Lys Leu Leu
    210                 215                 220

Asn Thr Leu Ser Arg Gln Ser Ala Ala Leu Thr Asn Glu Glu Arg Gly
225                 230                 235                 240

Leu Arg Gly Val Arg His Asn Ser Ser Leu Leu Gln Asp Gln Gln His
                245                 250                 255

Ser Leu Arg Gln Leu Leu Val Leu Leu Arg His Leu Val Gln Glu Arg
            260                 265                 270

Ala Asn Ala Ser Ala Pro Ala Phe Ile Met Ala Gly Glu Gln Val Phe
        275                 280                 285

Gln Asp Cys Ala Glu Ile Gln Arg Ser Gly Ala Ser Ala Ser Gly Phe
    290                 295                 300

Tyr Thr Ile Gln Val Ser Asn Ala Thr Lys Pro Arg Lys Val Phe Cys
305                 310                 315                 320

Asp Leu Gln Ser Ser Gly Gly Arg Val Thr Leu Ile Gln Arg Arg Glu
                325                 330                 335

Asn Gly Thr Val Asn Phe Gln Arg Asn Val Lys Asp Tyr Lys Gln Gly
            340                 345                 350

Phe Gly Asp Pro Ala Gly Glu His Val Glu Leu Gly Asn Glu Val Val
        355                 360                 365

His Gln Leu Thr Arg Arg Ala Ala Tyr Ser Leu Arg Val Glu Leu Gln
    370                 375                 380

Asp Val Glu Gly His Glu Ala Tyr Ala Gln Tyr Glu His Phe His Leu
385                 390                 395                 400

Gly Ser Glu Asn Gln Leu Tyr Arg Leu Ser Val Val Gly Tyr Ser Gly
                405                 410                 415

Ser Ala Gly Arg Gln Ser Ser Leu Val Leu Gln Asn Thr Ser Phe Ser
            420                 425                 430

Thr Leu Asp Ser Asp Asn Asp His Cys Leu Cys Lys Cys Ala Gln Val
        435                 440                 445
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Met Ser Gly Gly Trp Trp Phe Asp Ala Cys Gly Leu Ser Asn Leu Asn
450 455 460

Asp Val Tyr Tyr His Ala Pro Asp Asn Lys Tyr Lys Met Asp Gly Glu
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Arg Val His Tyr Phe Lys Gly Pro Ser Tyr Ser Leu Arg Ala Ser Arg
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Met Met Glu Arg Pro Leu Asp Glu
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